

contain all the essential elements of the anticipated claim. *Lindemann Maschinenfabrik v. American Hoist and Derrick*, 730 F.2d 1452, 1458, 221 USPQ 481, 485-86 (Fed. Cir. 1984); *Shanklin Corp. v. Springfield Photo Mount Co.*, 521 F.2d 609, 187 USPQ 129 (1st Cir. 1975). However, Applicants believe that a careful review of the '742 reference reveals that it fails to disclose salicylic acid, and therefore, fails to disclose an exfoliant. The present invention is the surprising discovery that cholesterol sulfate and an exfoliant, two agents having contra-activities, can be simply mixed together in a composition to enhance the protective barrier of the skin and/or repair the barrier if it has been damaged. This beneficial effect can be advantageously exploited on skin of all ages, and it is not disclosed by the '742 reference.

The '742 reference discloses a lipid vesicle which contains at least one salicylic acid derivative in a lipid phase forming the membrane of the vesicle. The salicylic acid derivative, according to the '742 reference, at column 3, lines 34 to 63, fortifies the lipid bilayer of the lipid vesicles and provides anti-acne activity. The Examiner points out that salicylic acid is a known exfoliant. However, the '742 reference discloses only derivatives of salicylic acid and not salicylic acid itself. There is no support in the '742 reference to indicate that the derivatives disclosed therein have any exfoliant activity at all, either alone or in combination with other actives. In fact, the '742 reference suggests that salicylic acid derivatives do not behave similarly, and therefore, provides reason for one of ordinary skill in the art to believe that salicylic acid derivatives would not behave like salicylic acid. At column 3, lines 44 to 54, the '742 reference discloses two salicylic acid derivatives that do not improve the physiochemical stability of vesicles and the encapsulation level. But, the particular salicylic acid derivative disclosed by the '742 reference allegedly achieves these benefits. Therefore, the '742 reference establishes that different salicylic acid derivatives behave differently, and therefore, there is no reason for one of ordinary skill in the art to believe that the particular salicylic acid derivatives of the '742 reference have exfoliant activity or any activity similar with that of salicylic acid. Thus, it can be seen that the '742 reference not only fails to disclose an exfoliant, but it also fails to inherently disclose an exfoliant. Therefore, the '742 reference fails to disclose the present invention, and Applicants respectfully request that the rejection under 35 U.S.C. §102(b) be withdrawn.

Further, the Examiner rejects Claims 1 to 4, 6 to 10, and 18 under §103 over the '742 reference in view of Subbiah, U.S. Patent No. 6,150,381 ("the '381 reference"). Obviousness is not found if the prior art fails to teach or suggest to one of ordinary skill in the art that the claimed invention should be carried out and if one of ordinary skill in the art would have no reasonable expectation of success making the claimed invention, as viewed in light of the prior art. *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,

18 USPQ2d 1016, 1022 (CAFC 1991); see *In re Dow Chemical Co.*, 837 F.2d 469 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Although it is known that compounds having structural similarity without more can give rise to *prima facie* obviousness, see, e.g., *In re Dillon*, 919 F.2d 688, 692-94, 16 USPQ2d 1897, 1900-02 (Fed. Cir. 1990) (tri-orthoesters and tetra-orthoesters), *cert. denied*, \_\_\_ U.S. \_\_\_, 111 S. Ct. 1682 (1991); *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (stereoisomers); *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977) (adjacent homologs and structural isomers); *In re Hoch*, 428 F.2d 1341, 166 USPQ 406 (CCPA 1970) (acid and ethyl ester), generalization is to be avoided insofar as specific structures are alleged to be *prima facie* obvious. *In re Jones*, 21 USPQ2d 1941, 1943 (CAFC 1992); *In re Grabiak*, 769 F.2d 729, 731, 226 USPQ 870, 872 (Fed. Cir. 1985).

The present invention is a simple mixture of an effective amount of an exfoliant and cholesterol sulfate. The combination of these two components has surprisingly been found to improve and/or protect the barrier of the stratum corneum even though the two components have opposite acting activities with respect to exfoliation. The present invention is not taught or suggested by the cited references nor would one of ordinary skill in the art reasonably expect to achieve the present invention based on the combination of the '742 reference and the '381 reference as discussed in further detail below.

The '742 reference teaches a lipid vesicle, and therefore, in addition to its failure to teach or suggest an exfoliant, as discussed above with respect to the novelty rejection, the '742 reference fails to teach or suggest the present invention of topically applying a simple mixture of two components, namely the cholesterol sulphate and the exfoliant. Lipid vesicles are formed, as disclosed at column 1, lines 46 to 54, of the '742 reference, by lipid membranes consisting essentially of concentric sheets of multimolecular lipid bilayers. The concentric layers are similar to the layers of an onion, and each layer is separated by an aqueous phase because the lipid layers swell in the presence of the aqueous solution and encapsulate the aqueous phase within the lipid layers. Therefore, within each of the layers there is a space wherein aqueous actives can be encapsulated. As a result of the ability to encapsulate actives, the vesicles act as a delivery system for the active, protecting and transmitting the active to a target.

Materials used to make the lipid membrane of the lipid vesicles are not simply mixed together. As presented in the '742 reference, at column 1, lines 33 to 37, there is a difference between the use of salicylic acid derivatives in emulsions, gels or lotions and the use of salicylic acid derivatives in lipid vesicles where the derivatives are part of the lipid membrane. The '742 reference specifically discloses, at column 1, lines 51 to 54, that amphiphilic lipids capable of forming vesicles are known to be ionic

amphiphilic lipids and/or non-ionic amphiphilic lipids. In particular at column 2, lines 33 to 35, the '742 reference discloses that the role of charged lipids, of which cholesterol sulphate is included as an ionic amphiphilic lipid, is to improve the stability of the vesicles by preventing their flocculation, as a consequent of their melting, even in the presence of an electrolyte. The presence of charged lipids also contributes to an increase in the encapsulation capacity of water-soluble substances by increasing the thickness of the aqueous layers separating the lipid sheets of the membranes of the vesicle, according to the '742 reference. The lipid vesicle requires specific processing steps to form the lipid bilayers and the internal cavity for encapsulation of the active. Therefore, the '742 reference establishes that lipid vesicles are distinct and separate entities from simple admixtures of components. The lipid vesicle is not a simple admixture of ingredients.

Unlike the compositions disclosed in the '742 reference, the cholesterol sulfate of the present invention is not in the context of a lipid vesicle but is part of a simple mixture with an exfoliant in a composition. Further, the '742 reference fails to disclose that a simple mixture of cholesterol sulfate and an exfoliant in a cosmetic composition has any benefit at all. The '742 reference fails to disclose that the derivatives would exhibit activity other than as an anti-acne agent. The lipid phase of the lipid vesicle forms many concentric layers of cavities each of which holds the aqueous phase similar to an apple filling held in the pastry dough of an apple turnover. A recipe for apple turnover containing a flour-derived substitute to fortify the pastry does not teach a simple combination of flour and apples nor does it teach any of the beneficial results that such a combination might have, presumably because it is not expected to have any. The present invention, however, has surprisingly found that by simply combining these two components, despite the fact that their activities are opposing with respect to exfoliation, a beneficial effect is achieved with respect to protecting the skin barrier. This is not recognized by the '742 reference, either alone or in combination with the '381 reference.

The '381 reference teaches sclareolide-like compounds for treating disorders caused by microbials such as, for example, bacteria, and one specific disorder is acne. As disclosed in the '381 reference, topical formulations containing sclareolide are generally prepared by admixing sclareolide in water and at least one organic solvent. Therefore, the '381 reference teaches that sclareolide is an aqueous active. Since the '742 reference teaches lipid vesicles encapsulating water soluble actives, the combination of these references at most suggests that sclareolide could be incorporated within the aqueous phase of the '742 lipid vesicles (i.e., sclareolide could be encapsulated). Because lipid vesicles

are not simple admixtures, the combination of the '742 reference and the '381 reference fails to teach or suggest the compositions of the present invention.

In addition, the Examiner finds that a combination of the '381 reference with U.S. Patent No. 5,650,166 issued to Ribier et al. ("the '166 reference") also renders the present invention obvious. However, the combination of these references likewise fails to teach or suggest the present invention because one of ordinary skill in the art would expect the sclareolide disclosed in the '381 reference, as with the previous combination of references, to merely be incorporated within the aqueous cavity of the lipid vesicles disclosed by the '166 reference, and therefore, be encapsulated.

The '166 reference teaches a moisturizing composition which comprises a first and a second dispersion of lipid vesicles. The first lipid vesicle penetrates, according to the '166 reference into the deep layers of the skin and contains at least one active. The '166 reference discloses at column 3, lines 66 to 67, that the lipid phase of the vesicles is an alkali metal salt of cholesterol sulphate. Therefore, the alkali metal salt of cholesterol sulphate is, similar to the '742 reference, disclosed as part of the lipid bilayer which forms the cavity within which an aqueous active is encapsulated. This, however as previously discussed, is not an admixture of cholesterol sulphate and an exfoliant as is the subject of the present invention, and therefore, the '166 reference also fails to teach or suggest the present invention. In addition to this, the combination of the '166 teachings with that of the '742 reference, similarly fails to teach or suggest the present invention because this combination only, at best, teaches that the aqueous phase can contain an aqueous active agent such as sclareolide in the cavity formed by the lipid bilayers of the lipid vesicle. Therefore, the combination of these two references fails to teach a mixture of the two components of the present invention, namely, the cholesterol sulphate and the exfoliant.

The lipid vesicle is not a mixture of components. Lipid vesicles are made of alternating layers of a lipid phase and an aqueous phase. The lipid phase encapsulating the aqueous phase carries and protects aqueous actives held by the aqueous phase within the cavity formed between the lipid phases. This is not the mixture of cholesterol sulphate and an exfoliant as described in the present invention for enhancing and protecting the protective barrier of the skin. A mixture of components is a random solution of components unlike a vesicle which is a discrete arrangement of its components. Because none of the cited references alone nor in combination would lead one of ordinary skill in the art to the compositions and methods of the present invention, a *prima facie* case of obviousness has not been established. Applicants request therefore, that the Examiner's rejection under §103 be withdrawn.

**CONCLUSION**

In view of the arguments presented above in the present submission, the claims are believed to be in condition for allowance, and issuance of a Notice of Allowance is respectfully solicited.

Respectfully submitted,

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# MARKED AMENDMENTS

12 (Amended). The composition of claim 1 further comprising both sclareolide and white birch extract.

20 (Amended). The method of claim 19 further comprising cholesterol sulfate or salts thereof in an amount of about 0.1 to 2.0 percent, about 0.5 to 8.0 percent of N-acetyl-D-glucosamine, cholesterol in an amount of about 0.2 to 1.0 percent, linoleic acid in an amount of about 0.2 to 1.0 percent by weight of the [of the] composition, sclareolide in an amount of about 0.001 to about 1.000 percent, and white birch extract in an amount of about 0.001 to about 1.000 percent.